Expression of the 2'-*N*-acetyltransferase gene in *Providencia stuartii* is controlled by multiple *trans* acting loci and cell to cell communication.

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The chromosomal 2'-*N*-acetyltransferase gene [*aac(2')-Ia*] is universally present in *P. stuartii* and encodes resistance to aminoglycosides. In wild-type *P. stuartii*, *aac(2')-Ia* transcription occurs at low levels. We have utilized transposon mutagenesis to identify insertional mutations resulting in constitutive, high-level *aac(2')-Ia* expression. These insertions have identified three *trans* acting loci, designated *aarA*, *aarC*, and *aarD*, which either directly or indirectly regulate *aac(2')-Ia* expression. In addition, *aac(2')-Ia* expression is also regulated by an extracellular factor, termed AR-factor, which acts in a cell to cell signaling pathway to decrease *aac(2')-Ia* expression. AR-factor is a small (below 3 Kd), heat and pronase resistant molecule, which begins to accumulate in cell supernatants at mid-log phase. Growth of *P. stuartii* in the presence of high AR-factor concentrations resulted in an 8-fold decrease in *aac(2')-Ia* expression. Although mutations which prevent the synthesis of AR-factor would be predicted to have increased *aac(2')-Ia* expression, the *aarA*, *aarC* and *aarD* mutants all produce wild-type levels of AR-factor. Interestingly, *aarD* mutants are unable to grow in the presence of AR-factor, suggesting this extracellular factor plays a critical role in *P. stuartii* growth under certain conditions.